

## Lipid Research

### GW25-e0429

#### Association between MLXIPL, BUD13 and ZNF259 gene polymorphisms and serum lipid levels in the Mulao and Han populations

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**Objectives:** The association of single nucleotide polymorphisms (SNPs) in the MLX interacting protein-like (MLXIPL), BUD13 homolog (BUD13) and zinc finger protein 259 (ZNF259) genes is inconsistent in diverse racial/ethnic groups. The present study was undertaken to detect the association of the MLXIPL (rs35332062 A358V, rs3812316 Q241H, rs13235543 P342P and rs799161 g.11092833T>C), BUD13 (rs10790162 +1741T>C, rs17119975 -575A>G and rs11556024 \*147C>T) and ZNF259 (rs2075290 -336G>A and rs964184 +359C>G) SNPs and serum lipid levels in the Guangxi Mulao and Han populations.

**Methods:** A total of 825 subjects of Mulao and 781 participants of Han Chinese were randomly selected from our previous stratified randomized samples. Genotyping of 9 SNPs was performed by polymerase chain reaction and restriction fragment length polymorphism combined with gel electrophoresis, and then confirmed by direct sequencing.

**Results:** The genotype and allele frequencies of ZNF259 rs2075290 and rs964184 and BUD13 rs10790162 were different between the Mulao and Han populations ( $P<0.001$ ). The SNPs of ZNF259 rs2075290 and rs964184, BUD13 rs10790162, and MLXIPL rs3812316 and rs13235543 were associated with serum triglyceride (TG); ZNF259 rs2075290 and BUD13 rs10790162 with total cholesterol; and MLXIPL rs35332062 with apolipoprotein (Apo) A1 in the Mulao population ( $P<0.006$ ). The SNPs of ZNF259 rs2075290 and BUD13 rs10790162 were associated with serum TG, and ZNF259 rs2075290 with ApoA1/ApoB ratio in the Han population ( $P<0.006$ ). Significant linkage disequilibrium was noted between ZNF259 rs2075290 and rs964184, ZNF259 rs2075290 and BUD13 rs10790162, ZNF259 rs964184 and BUD13 rs10790162, and MLXIPL rs3812316 and rs13235543 ( $r^2>0.50$ ,  $P<0.001$ ). Six haplotypes (among 5 SNPs of BUD13/ZNF259) and 7 haplotypes (among 4 SNPs of MLXIPL) with a frequency  $>1\%$  were identified in the Mulao and Han populations. We combined 17 haplotypes (among 5 SNPs of BUD13/ZNF259) and 13 haplotypes (among 4 SNPs of MLXIPL) with frequencies less than 3% into one group, called "rare\_hap". The A-C-G-A-C (among the ZNF259 rs2075290 and rs964184, and BUD13 rs10790162, rs17119975 and rs11556024 SNPs) and C-C-C-C (among the MLXIPL rs799161, rs35332062, rs3812316 and rs13235543 SNPs) haplotypes accounted for over half of the % haplotype of each ethnic group. Significant differences in the frequencies of the A-C-G-A-C and G-G-A-A-C haplotypes between the two ethnic groups were observed ( $P<0.01$  for each).

**Conclusions:** The present study shows that several SNPs in the MLXIPL, BUD13 and ZNF259 are associated with serum lipid parameters in the Guangxi Mulao and Han populations. But the association is different between the two ethnic groups. There may be an ethnic specific association of these SNPs and serum lipid parameters.

### GW25-e0567

#### The relationship between lipid-lowering efficacy, plasma concentrations and safety of short-term simvastatin and atorvastatin therapy with different dosages in Chinese population

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**Objectives:** We investigated the lipid-lowering efficacy of short-term simvastatin and atorvastatin therapy with different dosages of routine clinical practice, and studied the association of plasma concentrations, lipid-lowering efficacy and safety of simvastatin and atorvastatin in Chinese population.

**Methods:** 200 in-hospital patients with hypercholesterolemia were enrolled in the randomized controlled study. The patients were treated with daily doses of 20mg simvastatin, 40mg simvastatin, 10mg atorvastatin or 20mg atorvastatin orally each evening. The lipid profiles before and after 1-week treatment, as well as the plasma concentrations in the morning after 1-week treatment, which was 8 hours after last administration of simvastatin or atorvastatin, were assessed. All adverse events of simvastatin and atorvastatin were also recorded.

**Results:** Simvastatin and atorvastatin at each dose all effectively reduced TC and LDL-c levels from baseline to week 1 ( $P<0.001$ ). Simvastatin 20mg and simvastatin 40mg produced 17.5% and 24.6% reduction in LDL-c, respectively, and atorvastatin 10mg and atorvastatin 20mg produced 19.8% and 21.3% reduction in LDL-c, respectively. However, No differences were seen between different doses of simvastatin or atorvastatin. More patients at high risk in the study and in the 20mg atorvastatin group reached LDL-c target than those at very high risk (71% versus 32.8%,  $P<0.001$  for the overall patients; 80% versus 35.7%,  $P<0.05$  for 20mg atorvastatin group). There was no significant difference in the plasma concentrations between different dosages of simvastatin and atorvastatin. The plasma concentrations in 10mg atorvastatin group were correlated with the percent reduction of LDL-c ( $P<0.05$ ). No relationship was seen between the plasma concentrations and adverse events of simvastatin and atorvastatin.

**Conclusions:** Simvastatin and atorvastatin at different doses used by routine clinical practice can effectively reduce the TC and LDL-c levels after short-term treatment. Only the association between plasma concentration and lipid-lowering efficacy was seen in atorvastatin 10mg group. No association was observed between the plasma concentrations, efficacy and adverse events of simvastatin and atorvastatin in other groups.

### GW25-e1740

#### Contributing Factors of Weight Regain after Weight Loss in Ahvaz, Iran

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**Objectives:** Obesity is one of modifiable risk factors of cardiovascular diseases. Weight regain (WR) is very common among patients who lose weight. Physiological, psychological and behavioral factors are known to cause WR. Identifying the factors associated with WR in different populations is important. This study was carried out to identify the contributing factors of WR in Ahvaz, Iran.

**Methods:** In this case-control study, from clients referred to dietetics offices in Ahvaz, Iran from 2009 onwards, those older than 18 years and with no history of serious diseases such as cardiovascular diseases, diabetes mellitus, liver or kidney diseases and cancer were recruited. Overall 8000 files were investigated. All eligible clients who had lost at least 10 percent of initial weight and at least 6 months after their last appointments were invited to participate in this study. Weight maintainers (WM) were clients who had maintained their latest recorded weight or lower. WR was defined as regaining of at least 10 percent of the latest recorded weight. Seventy nine persons in the WR group were compared with 73 in WM group. Information about weight, age, sex, physical activities, breakfast consumption, specific changes in living conditions (e.g. divorce or death of relatives), hunger and overeating were collected from the file and by interview. Stress and depression were evaluated by DASS-21 questionnaire. Appropriate statistical tests, including Chi square and logistic regression were used for data analyses.

**Results:** Significant contributing factors of WR were inactive life style (less than 5 minutes walking per day and lack of regular exercise), depression or stress, inappropriate strategies (overeating) in confronting usual life problems, skipping breakfast, unrestrained eating, not to eat regular meals, and excessive hunger. According to multivariate logistic regression test, the significant predicting variables of WR were irregular consumption of meals and excessive hunger.

**Conclusions:** To prevent weight regain, diet therapy should be accompanied by behavioral, physical activity and psychological modifications.

### GW25-e2322

#### The Relationship Between Serum Lipids and BMI, WC, and WHR in Women in Shijiazhuang

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**Objectives:** To investigate serum lipid profiles in different age-related segments in women in Shijiazhuang and to evaluate the relationship between the serum lipids and body mass index (BMI), waist circumference (WC), and waist-hip ratio (WHR).

**Methods:** 1992 women were recruited in this study. Body height, body mass, body mass index (BMI), waist circumference (WC), hip circumference, waist-hip ratio (WHR) and serum lipid levels were measured in the morning after an overnight fast.

**Results:** The rate of dyslipidemia was increasing with the growing of age. The detection rates of high TC, high LDL-C, high TG and low HDL-C were 36.38%, 25.07%, 40.52% and 5.53%, respectively. There was no significant difference in lipid levels between age-related segments ( $P>0.05$ ). The levels of TC, TG and LDL-C increased with the growing of BMI. The levels of TC, TG and LDL-C were significantly higher in group of obesity than in group of normal BMI (TC:  $5.78\pm0.96$  mmol/L vs  $5.32\pm0.91$  mmol/L,  $P<0.05$ ; TG:  $1.98\pm0.59$  mmol/L vs  $1.17\pm0.38$  mmol/L,  $P<0.05$ ; LDL-C:  $3.27\pm0.44$  mmol/L vs  $2.86\pm0.57$  mmol/L,  $P<0.05$ ). The level of TG was significantly higher in population with abnormal WC and WHR than in population with normal WC and WHR ( $P<0.05$ ).

**Conclusions:** The rate of dyslipidemia was associated with age in women in Shijiazhuang. The levels of TC, TG and LDL-C was positively correlated with BMI. The level of TG was positively correlated with WC and WHR.

### GW25-e2344

#### Evaluation of apo A I, apo B, apo A I / apo B in the diagnosis of coronary heart disease

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**Objectives:** Whether the apo A I, apo B, apo I /apo B is relevant to the coronary atherosclerosis heart disease and Coronary artery lesion severity by statistical analysis, and the three level Coronary is evaluated how close to stenosis disease.

**Methods:** In January to March 2013, a total of 512 patients underwent coronary angiography according to the results of coronary angiography were divided into A, B,

C three groups. A group is the degree of coronary stenosis in 50% patients with a total of 108 cases. B group is the degree of coronary stenosis in patients with a total of 180 cases of 50%-70%. C group is the degree of coronary stenosis in 70% groups of patients with a total of 224 cases. Statistics of three groups of patients with clinical data and blood lipid levels, including apolipoprotein A I (apo A I), apolipoprotein B (apo B), apo A I / apo B analysis of the correlation between degree of the blood lipid and coronary artery stenosis.

**Results:** Compared between patients of group A and group B, apolipoprotein B (apo B) or apo A I / apo B was statistically significant ( $P<0.05$ ). Apolipoprotein A I (apo A I) is no statistical significance between the two groups. The mean level Apo B in B group increased than in A group, the mean level apo A I / apo B in A group increased than in B group.

Compared between patients of group A and group C, Apolipoprotein A I (apo A I), apolipoprotein B (apo B) or apo A I / apo B is all statistically significant ( $P<0.05$ ). The mean level Apo B in C group increased than in A group. The mean level of apo A I and apo A I / apo B in A group increase than in the C group;

Compared between patients of group B and group C, Apolipoprotein A I (apo A I), apolipoprotein B (apo B) or apo A I / apo B is all statistically significant ( $P<0.05$ ). The mean level Apo B in C group increased than in B group. The mean level apo A I and apo A I / apo B in B group increase than in the C group;

With the severity of coronary stenosis as the dependent variable, apo A I, apo B, apo A I / apo B as argument, the three are related with the degree of coronary artery stenosis by the method of multivariate regression analysis. The degree of apo B is positive correlation with coronary artery stenosis; apo A I and apo A I / apo B are negatively related to coronary artery stenosis. By the correlation coefficient, apo A I / apo B can be found most closely relationship between the degree of coronary stenosis and the following is apo A I, apo B.

**Conclusions:** With the severity of coronary stenosis, apo B increases, while apo A I and apo A I / apo B decrease. Apo A I / apo B correlation with coronary artery stenosis is the most close, followed by apo A I, apo B.

## GW25-e0425

### Polymorphisms in the BUD13 homolog and zinc finger protein 259 genes are associated with the risk of hyperlipidemia

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**Objectives:** The single nucleotide polymorphisms (SNPs) in the BUD13 homolog (BUD13) and zinc finger protein 259 (ZNF259) genes have been associated with one or more serum lipid parameters in the European populations. However, little is known about such association in the Chinese populations. The present study was undertaken to detect the association of 6 BUD13/ZNF259 SNPs and their haplotypes with hyperlipidemia and to identify the possible gene-gene interactions among these SNPs.

**Methods:** Genotyping of BUD13 237+1741T>C (rs10790162), 323-575A>G (rs17119975), \*147C>T (rs11556024), 64G>T (rs35585096) and ZNF259 1093-336G>A (rs2075290) and \*365+359C>G (rs964184) SNPs was performed in 634 hyperlipidemic (TC>5.17 mmol/L and/or TG>1.70 mmol/L) and 547 normolipidaemic individuals. Pair-wise linkage disequilibrium and haplotype frequencies among the SNPs were analyzed using Haploview. The association between genotypes and serum lipid parameters was tested by analysis of covariance. Any variants associated with the serum lipid parameter at a value of  $P<0.008$  (corresponding to  $P<0.05$  after adjusting for six independent tests by the Bonferroni correction) were considered statistically significant. Unconditional logistic regression was used to assess the correlation between the risk of hyperlipidemia and genotypes. The inter-locus interaction was analyzed by generalized multifactor dimensionality reduction method. A sign test or a permutation test provides P value for predicting accuracy to measure the significance of an identified model. The best model is selected as the combination of marker with maximum cross-validation consistency and minimum prediction error.

**Results:** The genotype distribution of all 6 SNPs agreed with Hardy-Weinberg equilibrium ( $P>0.05$  for all). A significant linkage disequilibrium was noted among the ZNF259 rs2075290, ZNF259 rs964184 and BUD13 rs10790162 SNPs ( $r^2>0.5$ ,  $P<0.001$ ). The SNPs of ZNF259 rs2075290, ZNF259 rs964184 and BUD13 rs10790162 were significantly associated with serum lipid levels in both hyperlipidemic and normolipidaemic populations ( $P<0.008$ - $0.001$ ). On single locus analysis, only BUD13 rs10790162 was associated with hyperlipidemia (OR: 2.23, 95% CI 1.05, 4.75,  $P=0.015$ ). The haplotype of A-C-A-G-C-C (in the order of the rs2075290, rs964184, rs10790162, rs17119975, rs11556024 and rs35585096 SNPs) was the commonest haplotype and represented approximately 50% of the sample. The haplotype of G-G-A-A-C-C, carrying rs964184-G-allele, was associated with increased risk of hypercholesterolemia (OR: 1.35, 95% CI 1.10, 1.66,  $P=0.005$ ) and hypertriglyceridemia (OR: 1.75, 95% CI 1.39, 2.21,  $P=0.000$ ). The haplotypes of A-C-G-G-C-C and A-C-A-G-T-C, carrying rs964184-C-allele, were associated with reduced risk of hypercholesterolemia (OR: 0.77, 95% CI 0.61, 0.99,  $P=0.039$  and OR: 0.66, 95% CI 0.47, 0.94,  $P=0.021$ , respectively). On multifactor dimensionality reduction analyses, the two-to-three locus models showed a significant association with hypercholesterolemia and hypertriglyceridemia ( $P<0.01$ - $0.001$ ).

**Conclusions:** The SNPs in the BUD13/ZNF259 in the European populations are also replicable in the Chinese populations. In addition, inter-locus interactions may exist

among these SNPs. However, further functional studies are still required to clarify how these SNPs and genes actually affect the serum lipid levels.

## GW25-e0066

### Excessive level of postprandial plasma glucose damage autonomic cardiovascular function and cardiac structure and function in elderly essential hypertensives

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**Objectives:** To explore the association between postprandial plasma glucose and autonomic cardiovascular function and cardiac structure and function in elderly essential hypertensives.

**Methods:** Oral glucose tolerance test were performed in 257 elderly essential hypertensives who were eligible recruited from health examination center affiliated to Institute of Basic Medicine, Shandong Academy of Medical Sciences. According to the results of oral glucose tolerance test, participants were divided into three groups, namely, normal postprandial plasma glucose group, high postprandial plasma glucose group and diabetes group. All participants were conducted physical examination, 24h ambulatory electrocardiogram, echocardiogram and blood test. Written informed consent was obtained from each patient.

**Results:** In normal postprandial plasma glucose group, high postprandial plasma glucose group and diabetes group, turbulence onset (TO) was  $-1.61\pm1.74\%$ ,  $-0.85\pm1.27\%$ , and  $0.16\pm0.91\%$ , respectively; total premature ventricular contraction of 24-hour was  $146.8\pm106.2$ ,  $302.2\pm200.6$ , and  $347.7\pm233.6$ , respectively; turbulence slope (TS) was  $10.36\pm5.59$  mm/RR,  $6.92\pm2.88$  mm/RR, and  $4.31\pm1.24$  mm/RR, respectively; the standard deviations of all normal RR intervals (SDNN) was  $98.54\pm22.83$  ms,  $87.40\pm24.74$  ms, and  $79.85\pm20.92$  ms, respectively; the end systolic diameters of left ventricle (LVESD) was  $25.36\pm2.28$  mm,  $26.33\pm2.07$  mm, and  $27.86\pm2.13$  mm, respectively; fractional shortening of the left ventricular minor semi axis (LVFS) was  $45.18\pm4.34\%$ ,  $43.36\pm4.14\%$ , and  $39.11\pm4.53\%$ , respectively; interventricular septum thickness (IVST) was  $9.11\pm0.86$  mm,  $9.57\pm1.12$  mm, and  $9.96\pm1.32$  mm, respectively; left ventricular posterior wall thickness (LVPWT) was  $9.06\pm1.03$  mm,  $9.17\pm1.05$  mm, and  $9.48\pm1.14$  mm, respectively; left ventricular ejection fraction (LVEF) was  $64.59\pm2.96\%$ ,  $59.02\pm3.12\%$ , and  $51.25\pm3.04\%$ , respectively; ratio of E/A was  $1.14\pm0.20$ ,  $1.07\pm0.23$ , and  $0.93\pm0.31$ , respectively; Tei index was  $0.34\pm0.09$ ,  $0.39\pm0.10$ , and  $0.44\pm0.10$ , respectively. Compared to normal postprandial plasma glucose group, TO, total premature ventricular contraction of 24-hour, LVESD, LVFS, IVST and Tei index were markedly elevated, and TS, SDNN, LVEF, and ratio of E/A were significantly decreased in high postprandial plasma glucose group and diabetes group ( $P<0.01$ ). TO, LVESD, LVPWT, and Tei index were significantly higher, and TS, LVEF, and ratio of E/A were significantly lower in diabetes group compared with high postprandial plasma glucose group ( $P<0.01$ ). Results of correlation analysis and multivariate linear regression analysis showed that level of postprandial plasma glucose markedly positively related to TO, total premature ventricular contraction of 24-hour, LVESD, IVST, LVPWT, A peak, and Tei index ( $r=0.422$ ,  $0.305$ ,  $0.418$ ,  $0.386$ ,  $0.285$ ,  $0.242$ , and  $0.440$ ,  $P<0.01$ , respectively), and negatively related to TS, SDNN, LVFS, LVET, E peak and ratio of E/A ( $r=-0.426$ ,  $-0.358$ ,  $-0.444$ ,  $-0.326$ ,  $-0.284$  and  $-0.403$ ,  $P<0.01$ , respectively).

**Conclusions:** Excessive level of postprandial plasma glucose damage autonomic cardiovascular function and cardiac structure and function in elderly essential hypertensives.

## GW25-e1622

### Cardiovascular inflammatory factors changes in patients with rheumatoid arthritis and intervention of atorvastatin

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**Objectives:** To observe the changes of cardiovascular inflammatory factors and to investigate the effect of atorvastatin therapy on inflammation in patients with rheumatoid arthritis (RA).

**Methods:** This study included 69 patients with RA, they were randomly divided into group A (n=36) and group B (n=33). All patients received methotrexate (MTX) 0.2 mg/kg/w, plus prednisone 10 mg /d and stable doses of NSAID therapy. Group A plus atorvastatin therapy (20 mg/d) on the basis of the above treatment. Sixteen healthy individuals of similar age and sex served as controls. Disease activity, lipid profile, C-reactive protein, serum tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), adiponectin were measured before and after 3 months of treatment.

**Results:** Atorvastatin combined with MTX therapy significantly reduced serum total cholesterol, low-density lipoprotein cholesterol, and triglycerides, TC/HDL-C, LDL-C/HDL-C, and increased high-density lipoprotein cholesterol. Disease activity variables, C-reactive protein, TNF- $\alpha$ , and adiponectin were significantly improved by the drug combinations.

**Conclusions:** Atorvastatin therapy in patients with RA reduced disease activity and conventional and novel vascular risk factors that promote the atheromatous lesion. Their possible mechanism may be benefited by the anti-inflammatory, the control of lipid, antioxidative stress, protecting vascular endothelium.